

REMARKS/ARGUMENTS

Claims 1, 3, 5, and 6 are pending in the application.

Claims 1, 3, 5, and 6 have been rejected under 35 U.S.C. § 103 (a) for alleged obviousness over Gallimore *et al.* Applicants disagree.

To establish a *prima facie* case of obviousness, three requirements must be satisfied: first, there must be some suggestion or motivation to modify the reference or to combine the reference teachings; second, there must be a reasonable expectation of success for achieving the claimed invention and its particular results; and, third, the prior art reference(s) must teach or suggest all the claim limitations. *See In re Vaeck*, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

Claims 1, 3, 5, and 6 are directed to methods for the purification of antigen-specific T cells by contacting a MHC class I protein-fluorescent protein *fusion* molecule or a *radiolabeled* MHC class I protein bound to a specific antigen with a population of T cells, incubating the MHC class I protein bound to the specific antigen together with the population of T cells for a time period sufficient for the T cells to internalize the MHC class I protein from the T cell surface, and identifying T cells that have internalized the MHC class I protein-fluorescent protein fusion molecule or the radiolabeled MHC class I protein.

An example of a MHC class I protein-fluorescent protein fusion molecule recited in the present claims is a MHC class I molecule fused to green fluorescent protein. *See, e.g.*, Specification as originally filed at page 4, lines 12-27. A fusion protein is defined in the art as “[t]he protein product of a gene *created by the fusion of two distinct genes.*” LEHNINGER *ET AL.*, in PRINCIPLES OF BIOCHEMISTRY, 2nd Edition, Worth Publishers, New York, 1993, G-6 (emphasis added). An example of a radiolabeled MHC class I protein recited in the present

claims is ^{35}S -labeled MHC class I protein. *See, e.g.*, Specification as originally filed at page 7, lines 16-29; Fig. 2C. It is these ***directly labeled*** MHC class I molecules that form complexes with, or bind to, antigen. Thus, the multimeric complexes internalized by the T cells in the methods recited in the claims include directly labeled MHC class I protein.

In contrast to the present invention, Gallimore *et al.* describes the use of class I-peptide complexes containing mouse class I heavy chain D^b bound to the LCMV peptide epitope glycoprotein (GP)33-41 and biotinylated human β_2 microglobulin ($\beta_2\text{M}$). As explained in that reference on page 1384 (“Protein Expression and Refolding”), the H-2 D^b molecule and the $\beta_2\text{M}$ molecule were independently expressed from separate vectors. Biotinylation of the $\beta_2\text{M}$ molecule was performed by incubation of $\beta_2\text{M}$ molecules with *N*-hydroxysuccinimide biotin. Complex formation was performed by coincubation of the biotinylated $\beta_2\text{M}$ molecules, the H-2 D^b molecules, and GP33-41. The complexes were subsequently fluorescent-labeled by coincubation with phycoerythrin-labeled neutravidin, which binds to the biotinylated $\beta_2\text{M}$ to form a tetrameric complex. *See Gallimore et al.*, page 1384, column 1. In other words, Gallimore *et al.* describes a labeled molecule complexed to a MHC class I protein bound in turn to antigen. No MHC class I-fluorescent protein fusion molecule or radiolabeled MHC class I molecule is described or suggested by Gallimore *et al.* Accordingly, Gallimore *et al.* cannot render obvious present claims 1, 3, 5, and 6.

Reliance on the statement in the present specification that “[i]t is also readily apparent to those of ordinary skill in the art that a variety of detectable markers, other than green fluorescent protein, can be fused to the MHC class I molecule, and are suitable for use in the methods of the present invention . . .” (Specification at page 4) to establish the alleged obviousness of the claimed methods is improper. It is a well-established principle of patent

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law that the teaching or suggestion to make the claimed modification and the reasonable expectation of success must both be found in the prior art, *not in applicant's disclosure*. See *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Accordingly, Applicants assert it is improper to rely on Applicants' disclosure to establish the motivation to modify the teachings of Gallimore *et al.* to arrive at the present invention or the likelihood of success of such a modification. Moreover, the level of skill in the art cannot be relied upon to provide the suggestion to combine or modify references. See *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 U.S.P.Q.2d 1161 (Fed. Cir. 1999).

Accordingly, Applicants respectfully submit that claims 1, 3, 5, and 6 are patentable over Gallimore *et al.* Applicants request reconsideration and withdrawal of the rejection.

Objections to Figures 1A, 1B, 1C, 1D, 1E, 2A, 2B, 2C, 2D, 3A, 3B, 3C, 3D, 4A, 4B, 4C, and 5 have been made. Applicants submit herewith replacement sheets of those figures. The figures have been amended to comply with 37 C.F.R. § 1.84. No new matter has been introduced by way of this amendment.

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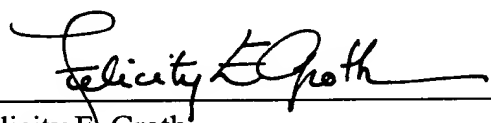
CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a Notice of Allowance at an early date is respectfully requested

If the Examiner believes a telephone conference would expedite prosecution of this application, the undersigned may be contacted at 215-557-5908.

Respectfully submitted,

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Attachments

Replacement sheets for Figures 1A, 1B, 1C, 1D, 1E, 2A, 2B, 2C, 2D, 3A, 3B, 3C, 3D, 4A, 4B, 4C, and 5
LEHNINGER *ET AL.*, in PRINCIPLES OF BIOCHEMISTRY, 2nd Edition, Worth Publishers, New York, 1993, G-6